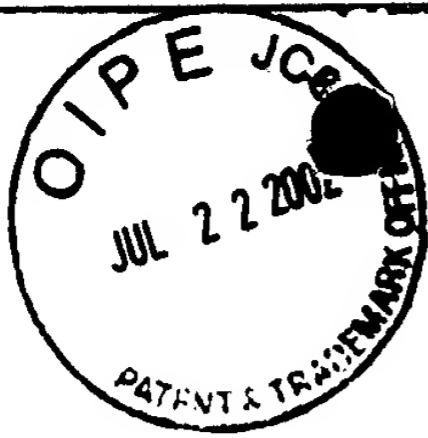


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Attorney Docket No.: A-68970-1/DJB/RMS/DCF

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

1634  
13/B  
CD  
7/31/02

In re application of:

FAN, et al.

Serial No. 09/785,514

Filed: February 16, 2001

For: PARALLEL GENOTYPING OF  
MULTIPLE PATIENT SAMPLES

) Examiner: CHAKRABARTI, ARUN K

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) Group Art Unit: 1634

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DC 20231 on 7-15-02

Signed:

*Kathleen J. Parrott*

**RESPONSE TO OFFICE ACTION**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

The following is in response to the office action (Paper No. 12) mailed April 15, 2002.  
The response is submitted on or before July 15, 2002, making this a timely response. The  
Commissioner is authorized to charge any additional fees which may be required, or credit any  
overpayment to Deposit Account No. 06-1300 ( Our Order No. A-68970-1/DJB/RMS).

Please make the following claim amendments and consider the following remarks.

## IN THE CLAIMS

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14. (Amended) A method comprising:

a) providing an array composition comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation each comprise a plurality of different target analytes;

wherein said microspheres are distributed on said surface;

b) contacting said array composition with a first set of readout probes;

c) detecting the presence of a first target analyte.

B1 15. The method according to claim 14 further comprising:

d) contacting said array composition with a second set of readout probes;

e) detecting the presence of a second target analyte.

16. The method according to claim 14, wherein said microspheres are randomly distributed on said surface.

17. The method according to claim 14, wherein said first set of readout probes comprises at least first and second readout probes, wherein said first and second readout probes comprise first and second labels, respectively.

18. The method according to claim 17, further comprising detecting said first label as an indication of the presence of said first target analyte.

19. The method according to claim 14, wherein the microspheres of said first and second subpopulation each comprise a plurality of target analytes from a first and second target source, respectively.

20. The array composition according to claim 19, wherein said first and second target source are first and second patients, respectively.

21. A method of genotyping comprising:

a) providing an array composition comprising:

- i) a substrate with a surface comprising discrete sites; and
- ii) a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation each comprise at least first and second target analytes attached to said microspheres with first and second attachment moieties, respectively;

wherein said microspheres are randomly distributed on said surface;

b) contacting said array composition with a first set of extension probes that hybridize with at least said first target sequence adjacent to a first detection position to form an extension complex;

c) contacting said extension complex with a composition comprising

- i) at least a first nucleotide;
- ii) polymerase;

wherein said polymerase extends a first extension probe with said first nucleotide when said first nucleotide is complementary to said first detection position of said first target sequence; and

d) detecting the presence of said first nucleotide.

22. The method according to claim 21, wherein said first nucleotide comprises a label.

23. (Amended) A method of determining the identification of a nucleotide at a detection position in at least a first target sequence comprising:

a) providing an array composition comprising:

- i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation each comprise a plurality of different target sequences, wherein said microspheres are distributed on said surface;

- b) forming a first hybridization complex between said first target sequence and at least a first readout probe; and
- c) determining the nucleotide at said detection position.

B1 24. A method according to claim 23, wherein said target sequence comprises a first and a second target domain, wherein said first hybridization complex comprises said first target sequence, a first readout probe hybridized to said first domain and a second readout probe hybridized to said second domain, wherein at least one of said readout probes comprise a label said determining comprises adding a ligase to form a ligation complex.

25. The method according to claim 24, wherein said first readout probe comprises a detectable label.

26. The method according to claim 23, further comprising contacting said hybridization complex with at least a first nucleotide and a polymerase, wherein said polymerase extends said first readout probe with said first nucleotide when said first nucleotide is complementary to said first detection position of said first target sequence.

27. (NEW) The method according to claim 14, 21 or 23 wherein said substrate is a fiber optic bundle.

B2 28. (NEW) The method according to claim 14, 21 or 23 wherein said substrate is selected from the group consisting of glass and plastic.

29. (NEW) The method according to claim 14, 21, or 23 further comprising contacting said microspheres with decoder binding ligands, wherein the microspheres of each subpopulation comprises an identifier binding ligand that will bind a decoder binding ligand for identification and elucidation of said target analyte.

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## **REMARKS**

Claims 14-29 are currently pending. Claim 14 and 23 have been amended. Support for the amendment of claim 14 and 23 is found in the specification at page 5, lines 9-10. Claim 21 has been renumbered as requested as requested by the Examiner. Claim 23 has been amended. Support for the amendment of claim 23 is found in the specification at page 10, lines 17-26. Claims 27-29 have been newly added. Support for new claim 27 is found in the specification at page 9, lines 19-23. Support for new claim 28 is found in the specification at page 10, lines 20-21. Support for new claim 29 is found in the specification at page 18, lines 13-32; pages 19-20; page 21, lines 1-23. A "clean" claim set to replace the original claims is provided above. A version showing changes made is attached hereto for the Examiner's convenience. An appendix of pending claims is also provided for the Examiner's convenience.

### **Double Patenting Rejection**

Claims 14-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 6, 355,431 B1.

Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

### **Rejections based under 35 U.S.C. § 102**

Claims 14-26 are rejected under 35 U.S. C. § 102(e) as being anticipated by Beattie et al. (U.S. Patent 6,268,147 B1).

Beattie et al. is directed to nucleic acid analysis using sequence targeted tandem hybridization. Tandem hybridization involves hybridizing a labeled stacking probe to a particular sequence within the target and then subsequently or even simultaneously hybridizing an unlabeled capture probe which is tethered to a substrate. Beattie et al. does not teach microspheres distributed on a surface. Nor does Beattie et al. teach contacting array compositions with extension probes, at least a first nucleotide and a polymerase, which is performing extension reactions on microspheres distributed on a surface ( claim 21). Beattie et al. discloses performing PCR reactions prior to analyzing PCR products using tandem hybridization methodology ( column 31, lines 50-67, column 32, lines 1-19; column 38, lines 60-67, column 39, lines 1-6).

In contrast, the claims of the Applicant's invention are directed to analyzing nucleic acid sequences using microspheres distributed on a surface ( claims 14 and 23) and providing for a method of genotyping by performing extension reactions by contacting microspheres with attached target analytes and extension probes with at least a first nucleotide and a polymerase (claim 21). In addition, the claims are directed to microspheres comprising more than one target analyte (claim 14 or 23).

The law is well established that in order to anticipate a claim, the prior art must disclose "each and every element" of the claimed invention. SSIH Equipment S.A.v. U.S. Inc. Int'l. Trade Commission, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." (Emphasis added). See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1496 (Fed. Cir. 1995).

Although Beattie et al. discloses bead technology, it does not disclose the use of beads or microspheres distributed on a surface, which is an element of the claims of the present invention. In addition, Beattie et al. fails to disclose microspheres comprising more than one target analyte, which is an element of claims 14 and 23.

Beattie et al. does not disclose each and every element of the claimed invention. Accordingly, Beattie et al does not anticipate the present claims and the rejection is improper. Applicants respectfully request the withdrawal of the rejection.

Applicants submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

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Dated: 7/19/02

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